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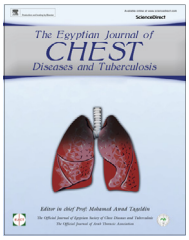

CASE REPORT

Migratory pneumonia caused by common variable immunodeficiency disorder

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KEYWORDS

Pneumonia;
Bronchiectasis;
Common variable immunodeficiency;
Hypogammaglobulinemia

Abstract Recurrent respiratory infections are important causes for bronchiectasis which can also be caused by a severe or poorly treated single infective event. With the widespread usage of vaccines for whooping cough and measles and the efficacy of anti-tuberculosis chemotherapy, the latter cause has receded as predisposing factor to developing bronchiectasis especially in the developed world. Primary antibody deficiency syndromes (PADS) are uncommon causes for recurrent respiratory infections and bronchiectasis. The importance of a timely diagnosis of such conditions is that treatments are available and can prevent the development of bronchiectasis. I here report the case of a young gentleman who suffered from recurrent pneumonias for seven years before identifying common variable immunodeficiency disorder as the underlying disease.

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Case report

A 26 year-old male presented with a 3 day history of fever, productive cough of purulent sputum and right-sided stitching chest pain. By examination, the patient looked pale, dehydrated and underweight. Macular rash, which the patient did not notice before, was noted in both lower limbs. Blood pressure was 110/60 mmHg, respiratory rate was 24 bpm and heart rate was 118 bpm and temperature was 39.5 °C. Chest examination revealed signs of consolidation overlying the middle lobe. The patient gave a long history of recurrent sinus infections and diarrhea as well as repeated hospital admissions for respiratory infections. Laboratory investigations were within normal limits except for mild leucocytosis with neutrophilia and a high CRP level. Sputum culture was sterile. The oldest radiology the patient possessed was a chest CT dating from 2007 (Fig. 1A) showing middle lobe consolidation and mild bronchiectatic changes in the left lower lobe. A new chest X-ray (Fig. 1B) showed a middle lobe consolidation. Given the previous history of a similar consolidation, a fiberoptic bronchoscopy was performed to evaluate the structure of the right bronchial tree. No abnormalities could be detected. The patient improved on empirical antibiotics with normalization of the CRP and white cell count. Drug reaction was suggested as the cause for skin lesions. Six months later, the patient presented with similar symptoms. Chest X-ray revealed right lower lobe consolidation with effusion (Fig. 1C). Sputum and pleural fluid cultures were sterile. Bronchoscopy was repeated to perform a bronchoalveolar lavage (BAL) for cellular and microbiolog-

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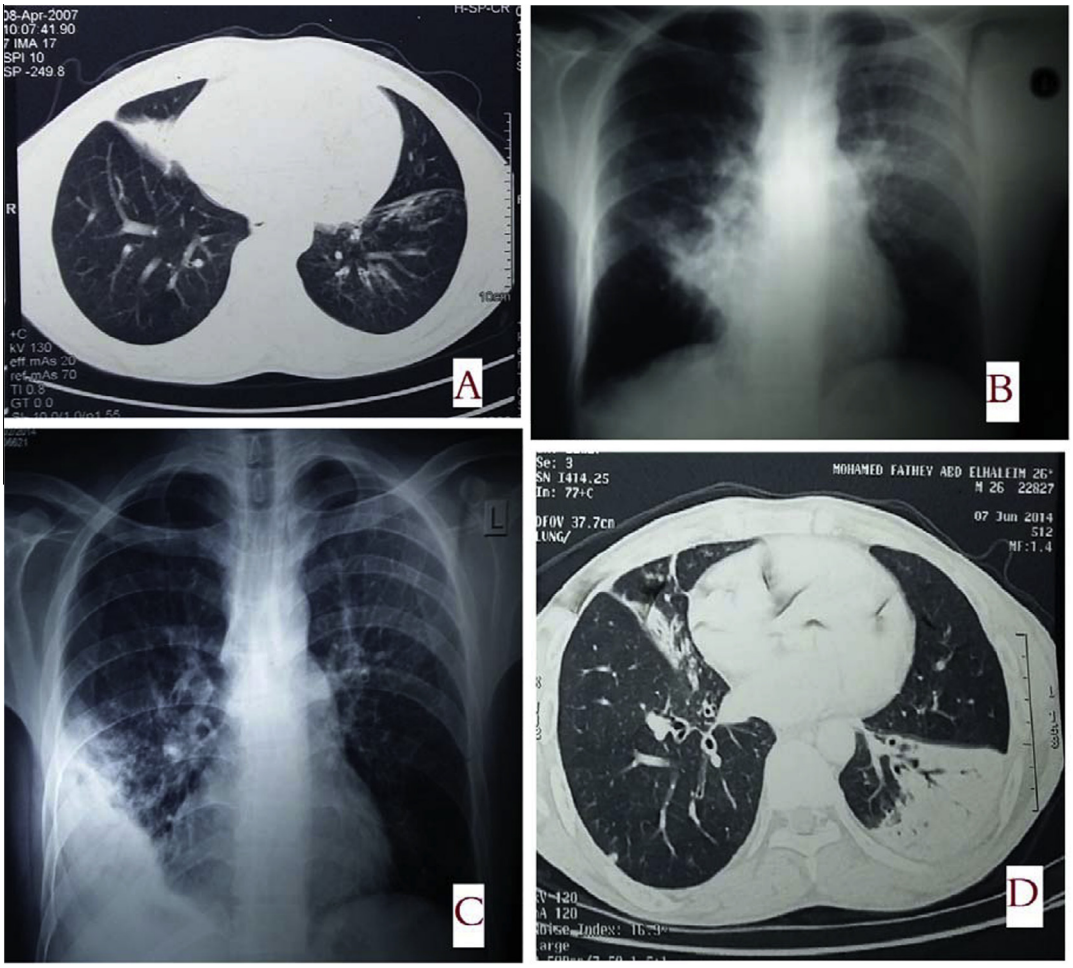

Figure 1 (A) Chest Ct shows middle lobe consolidation, and minimal bronchiectasis at left lower lobe. (B) Chest X-ray: middle lobe consolidation. (C) Right lower lobe consolidation with effusion. (D) Left lower lobe consolidation, with middle lobe bronchiectasis.

ical analysis. Cultures for bacteria, mycobacteria and fungi were all negative. Cellular analysis revealed predominance of neutrophils. After improvement, patient was discharged with the advice to receive influenza and pneumococcal vaccine. The patient came back 3 months later with pneumonia in the left lower lobe. In addition to the left lower lobar consolidation, the chest CT (Fig. 1D) showed cylindrical bronchiectasis in the right middle and lower lobes. Immune deficiency was suspected, and given the normal white cell count, a humoral component was sought. Serum protein electrophoresis (Fig. 2) confirmed the presence of hypogammaglobulinemia. Serology for HIV, HCV, HBV infections, rheumatoid arthritis and systemic lupus were all done to exclude a secondary cause for hypogammaglobulinemia. Results were all negative. An abdominal ultrasound revealed splenomegaly. Very low levels of IgM (<0.05 g/L) and IgG (<0.3 g/L) were recorded. Given these findings of repeated infections, low levels of antibodies and poor response to vaccination, the diagnosis of common variable immunodeficiency disorder (CVID) was made. The skin lesions were diagnosed as cutaneous granulomas which, together with splenomegaly, are recognized complications of CVID. Intravenous immunoglobulins (IVIGs) were prescribed to prevent recurrence of infection. It is hoped that following a proper treatment regimen will halt the progression of the structural lung damage.

Discussion

Antibodies (immunoglobulins) are synthesized by plasma cells, which are themselves the result of the development and differentiation of B lymphocytes. Any cause that inhibits the development of the B cell lineage or its function as a mature cell may result in decreased levels of serum immunoglobulins (hypogammaglobulinemia) [1].

Primary antibody deficiency syndromes (PADS) comprise a wide variety of disorders characterized by defective antibody production in response to microbes, resulting in recurrent infections in the sinopulmonary tract and the gastrointestinal tract. Recurrent pulmonary infections lead eventually to bronchiectasis. In addition, patients with common variable deficiency (CVID), one of the frequent forms of PADS, may develop inflammatory lung disease, often associated with multi-system granulomatous disease [2]. PADS fall into either of two groups: a group of disorders with well-identified genetic alterations (e.g. X-linked agammaglobulinemia and autosomal recessive agammaglobulinemia) and

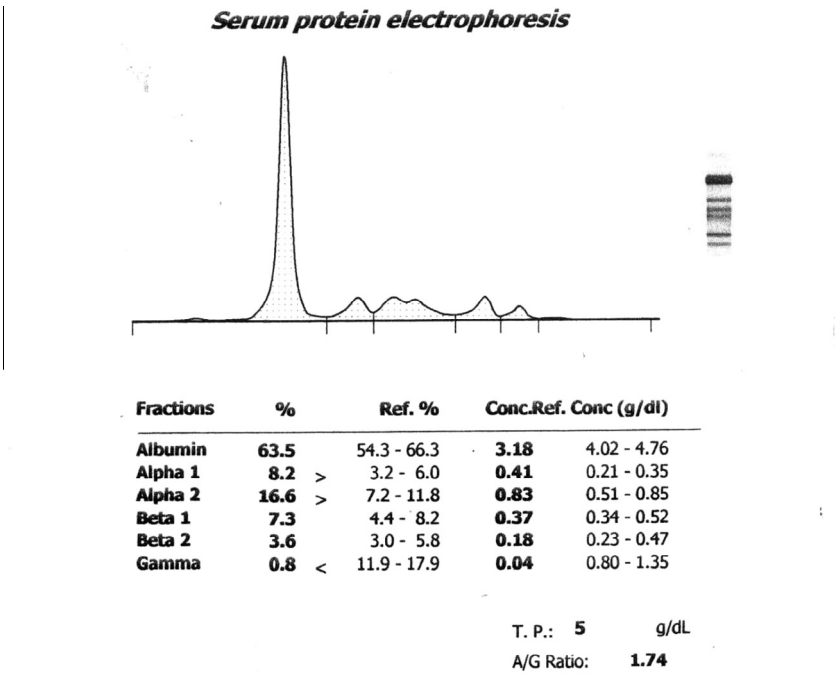

Figure 2 Serum protein electrophoresis shows hypogammaglobulinemia.

another group with unknown genetic background. The latter group constitutes the largest one and includes CVID, IgG subclass deficiencies, IgA deficiency, and selective antibody deficiency [3].

Before diagnosing a primary antibody deficiency disorder, secondary causes for antibody deficiency need to be excluded. These conditions include: prolonged courses of glucocorticoids and immunomodulatory drugs, surgery and trauma, extreme environmental conditions, profound metabolic abnormalities, autoimmune diseases and chronic infections, such as those caused by HIV [4].

CVID is the archetype of PADS and is characterized by impaired B cell differentiation with defective immunoglobulin production. It is the most prevalent form of severe antibody deficiency affecting both children and adults with an estimated prevalence of 1 in 25,000 individuals [5], hence the term "common." Variability of the presentation, as the name implies, is manifested by heterogenous presentations, including recurrent infections, chronic lung disease, autoimmune disorders, gastrointestinal disease, and an increased susceptibility to lymphoma [2]. The age of onset is typically after puberty and before 30 years of age, with some evidence of a bimodal distribution demonstrating peaks between 1 and 5 years, and 18 and 25 years [6]. CVID is defined by the triad of: (a) markedly reduced serum concentrations of IgG, in combination with low levels of IgA and/or IgM, (b) poor or absent response to immunization and (c) absence of any other defined immunodeficiency state [6]. Sinopulmonary infections, including pneumonia, bronchitis, and sinusitis, as well as otitis and conjunctivitis, are observed in the majority of patients with CVID. These infections may be acute, chronic, or recurrent. Patients are particularly susceptible to infection with Pneumococcus, Hemophilus, and Mycoplasma species [7]. Diarrhea also occurs very commonly, with malabsorption and weight loss also reported [5]. Bronchiectasis, defined as irreversible dilatation of large and medium-sized bronchi, is one of the most feared complications of the repeated pyogenic respiratory infections affecting CVID patients. The presence of bronchiectasis at diagnosis predicts poor outcome, while early diagnosis and aggressive management predicts good outcome [8].

The presentation of CVID might mimic other famous causes of bronchiectasis like primary ciliary dyskinesia (PCD) and cystic fibrosis (CF). PCD is associated frequently with infertility and nose/sinus problems since infancy. CF can be diagnosed with a positive chloride sweat test as well as genetic testing. Antibody deficiency is not demonstrable in both of these conditions.

The treatment of CVID is centered on preventing the recurrent respiratory infections from inflicting irreversible structural lung damage. This is achieved via the two cornerstones of management; intravenous replacement of immunoglobulins (IVIG) and timely eradication of respiratory infections. Early identification and aggressive management of pyogenic infections with prolonged courses on antibiotics will guard against development of bronchiectasis. Immunoglobulin is administered intravenously every 2–4 weeks or subcutaneously every 1–2 weeks, with a usual starting dose of 0·4–0·6 g/kg/month [9]. To date, routine antibiotic prophylaxis is not recommended. Some authors however advocate prophylactic antibiotics in patients with recurrent infections despite adequate IG replacement. The proposed regimen is based on macrolide antibiotics due to their anti-inflammatory as well as antimicrobial properties, with prescription frequency similar to that of CF (500 mg tab, 3 times a week) [2].

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